CASE REPORT

Dengue shock syndrome in an infant

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SUMMARY

Dengue is a mosquito-borne infection affecting children and adults worldwide. In newborn infants, the dengue virus can cause diseases, especially in infants born to pregnant women hospitalised with dengue or postpartum women with fever. The authors report a case of a term newborn infant who presented with haemodynamic instability and thrombocytopaenia at the age of 7 days, without a history of clinical dengue infection in the mother. The physical examination revealed an afebrile and drowsy infant with a petechial rash all over the body and ecchymosis on both palms and soles. The authors confirmed the diagnosis using the dengue NS1 antigen on the first day of admission. The treatment included fluid management and platelet transfusion. The patient recovered well and was discharged from the hospital on the 10th day of hospitalisation.

BACKGROUND

Dengue is a mosquito-borne infection affecting children and adults worldwide; it has become a major International Public Health concern in recent decades. According to estimates by the WHO, approximately 50–100 million dengue infections occur worldwide each year.¹ While there are four distinct, but closely related, serotypes of the virus that cause dengue (DEN-1, DEN-2, DEN-3 and DEN-4), a previous infection by one of these serotypes provides lifelong immunity against that particular serotype. However, cross-immunity to the other serotypes after recovery is only partial and temporary, and subsequent infections by other serotypes increase the risk of developing severe dengue.²

In Thailand, dengue haemorrhagic fever, or severe dengue, is among the leading causes of hospitalisation and death among children. Its severity ranges from a mild flu-like illness to potentially life-threatening complications from plasma leaking, fluid accumulation, respiratory distress, severe bleeding or organ failure. In general, dengue would be suspected when a child presents with the classic syndrome of high fever accompanied by severe headache, myalgia, nausea, vomiting, swollen lymph nodes or rash. The incubation period from the time of a bite of an infected mosquito is around 4–10 days and symptoms last for 2–7 days. The diagnosis is usually carried out on clinical grounds, either with or without confirmatory laboratory results. Nevertheless, in infants, the manifestations may not be typical, as in older children, which can make the diagnosis more challenging. We now report a rare case of a newborn

infant with clinical symptoms of dengue shock syndrome.

CASE PRESENTATION

A 7-day-old female newborn was transferred to our hospital from a local healthcare centre due to drowsiness and low-grade fever for 1 day. Her mother was a 20-year-old primigravida with an uneventful antenatal history; no medical or obstetric complications were noted. The infant was delivered at the gestational age of 38 weeks. Her birth weight was 2695 g (appropriate for gestational age) and the Apgar scores were 9 and 10 at 1 and 5 min, respectively. The baby was healthy and discharged from the hospital with her mother 3 days after birth. On the scheduled baby clinic visit 1 week after birth, her mother reported that the baby had a lethargic appearance, drowsiness, and poor feeding for 1 day. She also noticed that the infant's hands and feet were cyanotic. The physical examination revealed a drowsy infant with response to stimuli, loud crying, non-tense anterior fontanelle (2×2 cm), body temperature of 37.5°C, regular heart rate, normal respiratory pattern and normal breath sound. A petechial rash was observed all over the body with ecchymosis on the palms and soles (figures 1 and 2). The capillary refill time was 2 s. No obvious bleeding was found. The preliminary diagnosis was late neonatal sepsis with thrombocytopaenia. A complete blood count showed haemoglobin of 16 g/dL, haematocrit 51%, white cell count 7250 cells/mm³ (27% neutrophils, 49% lymphocytes, 6% atypical lymphocytes and 18% monocytes) and platelet count 6000/mm³. She was transferred to our hospital for haematological consultation and intensive neonatal care.

On the day of admission, the physical examination revealed a body weight of 2780 g, length 49.4 cm, temperature 37°C (normal range 36.5–37.5°C), respiratory rate 56 breaths/min (normal range 40–60 breaths/min), pulse rate 130 bpm (normal range 100–160 bpm), blood pressure 64/39 mm Hg (normal range 76/46 mm Hg) and mean arterial pressure 47 mm Hg (normal range 58 mm Hg).

INVESTIGATIONS

The laboratory results on the day of admission showed a haemoglobin level of 16.5 g/dL (normal range 12.7–18.3 g/dL), haematocrit 50.3% (normal range 37.4–55.9%), total white cell count 5135 cells/mm³ (normal range 5,000–21 000 cells/mm³) (27% neutrophils, 56% lymphocytes and 13% monocytes) and low platelet count 22 000/mm³ (normal range 150 000–350 000/mm³). The

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Figure 1 Ecchymosis on palm of the left hand.

Figure 2 Ecchymosis on sole of the right foot.

arterial blood gas revealed metabolic acidosis. The liver function test showed an elevated aspartate aminotransferase (AST) level of 114 U/L (normal range 20–60 U/L), a normal level of alanine aminotransferase (ALT) 20 U/L (normal range 2–25 U/L), low albumin level of 2.6 g/dL (normal range 2.7–4.3 g/dL) and normal level of total bilirubin 3.02 mg/dL (normal range <13 mg/dL). Other investigations showed a high normal prothrombin time of 13 s (normal range 10.9–13.9 s), prolonged partial thromboplastin time 80.3 s (normal range 34.0–51.2 s), low fibrinogen level 104 mg/dL (normal range 200–500 mg/dL) and C reactive protein level <3.3 mg/L (normal range 10–350 mg/L).

A blood non-structural protein antigen (dengue NS1 antigen) was positive since the first day of admission. The patient's dengue-specific IgM antibody was also positive. Her mother's blood tests were positive for dengue IgG and IgM antibodies. However, we did not test for the serotype of the dengue virus in either mother or child because our hospital did not have this test.

Chest radiography showed neither cardiomegaly nor pleural effusion.

DIFFERENTIAL DIAGNOSIS

The most likely diagnosis was dengue shock syndrome and the differential diagnosis also included late neonatal sepsis with suspected meningitis.

TREATMENT

On the day of admission, the initial management included two consecutive doses of normal saline (15 mL/kg) and platelet concentration transfusion (10 mL/kg). In this case we decided on platelet transfusion because of the extensive ecchymosis and low platelet count ($18\,000/\text{mm}^3$) as well as bleeding via the umbilical stump after the umbilical catheterisation. The platelet count increased from $22\,000$ to $77\,000/\text{mm}^3$. The additional treatment comprised of 5% D/NSS/5 (total volume: 150 mL/kg) and empirical antibiotics (ampicillin and cefotaxime: meningitis dose).

On the second day of admission, the platelet count decreased to $9000/\text{mm}^3$ and two consecutive doses of platelet concentration (10 mL/kg/dose) were given. A lumbar puncture was performed and normal protein and sugar profiles were found. Decreased urine output was observed, and fluid loading with normal saline was prescribed. The infant was fed with breast milk, and she could suck well.

On the third day of admission, another dose of platelet concentration (10 mL/kg) and intravenous furosemide were given. Maintenance fluid was reduced as the infant was well fed with breast milk.

On the fourth day of admission, cefotaxime dosage was reduced from a meningitis treatment dose to a sepsis treatment dose as the cerebrospinal fluid culture showed no growth of bacteria. Latex agglutination was negative.

OUTCOME AND FOLLOW-UP

This baby recovered well after platelet transfusion and supportive treatment. She had neither obvious bleeding nor following haemodynamic instability. Her petechiae and ecchymosis gradually faded and her appetite was normal. She was discharged from our hospital on the 10th day of hospitalisation. On her follow-up visit, 2 weeks after discharge from the hospital, petechiae and ecchymosis had completely disappeared.

DISCUSSION

We report a case of a term newborn infant who presented with haemodynamic instability and thrombocytopaenia at the age of 7 days without a history of clinical dengue infection in the mother. The diagnosis of dengue infection was confirmed by an antigen test during admission. Despite the late diagnosis, prompt treatment was provided and the infant recovered well.

Even though dengue viral infection has been endemic in Thailand for years, it mostly affects school-age children. Dengue in children ≤ 2 years of age constituted 2.9% and 7.7% of dengue infections in children as reported from two different hospitals in Thailand.^{3 4} Dengue haemorrhagic fever and dengue shock syndrome in infants less than 1 year of age accounts for 5% of children hospitalised with dengue disease in this region.³ In recent years, more adolescent and young adult cases were seen; thus, women in their reproductive age are at risk. Dengue disease in infants could be either from vertical transmission or primary dengue infection; its manifestation could be severe as these infants might have received dengue antibodies transplacentally from their mother.⁵

In most reported cases, dengue infections in newborn infants were anticipated as they were born to pregnant women hospitalised with dengue,^{6 7} or postpartum women with fever.⁸ When infants were born to mothers with clinical dengue infection or were found to have fever prior to the hospital discharge after birth, vertical transmission was suspected. However, in this case there was a possibility that the infant got infected after birth through a mosquito bite at home in the first few days of life after discharge from hospital.

Dengue cases in infants are at risk of being underdiagnosed, as the presentation and clinical features may not be distinct from other types of neonatal infections, such as bacterial and viral infections. In general, physicians can recognise dengue infection in infants by looking at the history of illness in the mother. However, when the mother's illness is subtle, the diagnosis of dengue in infants may be more difficult.

Some clinical manifestations, which were reported in infants more often than in older children, include liver involvement (mean AST/ALT) elevation and prolonged prothrombin time)⁹ and thrombocytopaenia.¹⁰ Basically, newborn infants have physiological haemoconcentration; haematocrit could be as high as 56% at the age of 1–3 days and gradually decline after 6 weeks; physiological anaemia occurs at around 3 months of age.¹¹ Thus, the sign of haemoconcentration may not be helpful for the diagnosis of dengue in infants.

In this case, since we were aware of the likelihood of dengue infection due to the common outbreaks of this disease in our region, we confirmed the diagnosis through a dengue NS1 antigen test. This test has been recently used in diagnosing early dengue infection before dengue-specific antibodies can be detected; however, it is more costly and not widely available in Thailand. In our hospital, we detected early dengue infection with SD BIOLINE NS1/IgM/IgG which has a sensitivity of 80.7% (95% CI 75% to 85.7%) with likelihood ratios of 7.4 (95% CI 4.1 to 13.8) and 0.21 (95% CI 0.16 to 0.28).¹²

At the end of the acute phase of infection, serology is the most commonly used diagnostic method. IgM antibodies are the first immunoglobulin isotypes to appear in one half of cases by days 3–5 after onset of illness and reach their peak by 2 weeks. Serum IgG will increase later but remains detectable for several months or longer.¹³ Later on in our case, serological testing was

performed in both mother and infant, and the results supported primary infection in the infant and secondary infection in her mother.

As the case was diagnosed after the febrile phase, treatment mainly provided for haemodynamic instability, including fluid management, and empirical antibiotic treatment was prescribed to cover neonatal meningitis as well as late neonatal sepsis, which could not initially be ruled out. Platelet transfusion was indicated as there were clinical petechiae, ecchymosis and coagulopathy.

In conclusion, in regions where dengue is endemic, physicians should be aware that dengue infection can occur in newborn infants as well. It should be included in differential diagnosis lists. Timely investigations as well as appropriate management are needed to prevent morbidity and mortality.

Learning points

- ▶ In endemic regions of dengue infection, physicians should be aware of dengue infection in every age group including newborn infants.
- ▶ Early detection, prompt diagnosis as well as appropriate management in dengue infection are needed to prevent morbidity and mortality.
- ▶ Appropriate initial treatment in dengue shock syndrome in newborn infants includes early fluid resuscitation and platelet transfusion in case of clinical petechiae and ecchymosis, such as in this patient.

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Competing interests None.

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